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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/565,557	01/23/2006	Russell J. Thomas	283569US0PCT	2098

22850 7590 04/25/2007
OBLON, SPIVAK, MCCLELLAND, MAIER & NEUSTADT, P.C.
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ALEXANDRIA, VA 22314

EXAMINER

LOEWE, SUN JAE Y

ART UNIT	PAPER NUMBER
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1609

SHORTENED STATUTORY PERIOD OF RESPONSE	NOTIFICATION DATE	DELIVERY MODE
3 MONTHS	04/25/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Notice of this Office communication was sent electronically on the above-indicated "Notification Date" and has a shortened statutory period for reply of 3 MONTHS from 04/25/2007.

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Office Action Summary

Application No.

10/565,557

Applicant(s)

THOMAS ET AL.

Examiner

Sun Jae Y. Loewe

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 March 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4 and 6-28 is/are pending in the application.
- 4a) Of the above claim(s) 1-4, 6-9, 18 and 22-28 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 10-17 and 19-21 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date 4/19/2006.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group II, and compound 5-[(3-cyclopentylpropanoyl)(4- {[(4-phenoxybenzyl)amino]carbonyl}benzyl)amino]-2-hydroxybenzoic acid, in the reply filed on March 3, 2007 is acknowledged. The traversal is on the ground(s) that the search of all claims would not constitute a serious burden. Therefore, based on MPEP § 803, the restriction requirement was stated to be improper. This is not found persuasive for the following reason.

The instant case is a national stage application submitted under 35 U.S.C. 371, therefore Unity of Invention practice in MPEP § 1850 and MPEP § 1893.03(d) was followed. It was shown in the restriction requirement mailed on March 1, 2007 that: (i) the inventions divided as Groups I, II, and III lack unity of invention as defined in PCT Rule 13.2 (see p.2) and; (ii) the Markush products of Formula I, within each of Groups I-III, did not fulfill the criteria of being of similar nature (MPEP § 1850.III.B) and thus lack the special technical feature as defined in PCT Rule 13.2 (see pgs. 2-3). For these reasons, the restriction requirement mailed on March 1, 2007 is still deemed proper and is made FINAL.

Applicant's elected compound, 5-[(3-cyclopentylpropanoyl)(4- {[(4-phenoxybenzyl)amino]carbonyl}benzyl)amino]-2-hydroxybenzoic acid, was found to be allowable. Thus, the search and examination was extended to the full scope of the subject matter in claims 10-17 and 19-21 (Group II). The non-elected inventions in Groups I and II were not rejoined per MPEP § 1893.03(d) because the full scope of the invention in Group II was not found to be allowable (see below sections 5 and 6)

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2. Claims 1-4, 6-9, 18, 22-28 withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions. Applicant timely traversed the restriction (election) requirement in the reply filed on March 3, 2007.

Priority

3. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Information Disclosure Statement

4. The information disclosure statement (IDS) submitted on April 19, 2006 was in compliance with the provisions of 37 CFR 1.97 and 37 CFR 1.98. Accordingly, the information disclosure statement was considered. A signed copy of form 1449 is enclosed herewith.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

(Written Description)

The analysis of whether the specification complies with the written description requirement calls for the comparison of the scope of the claim with the scope of the description

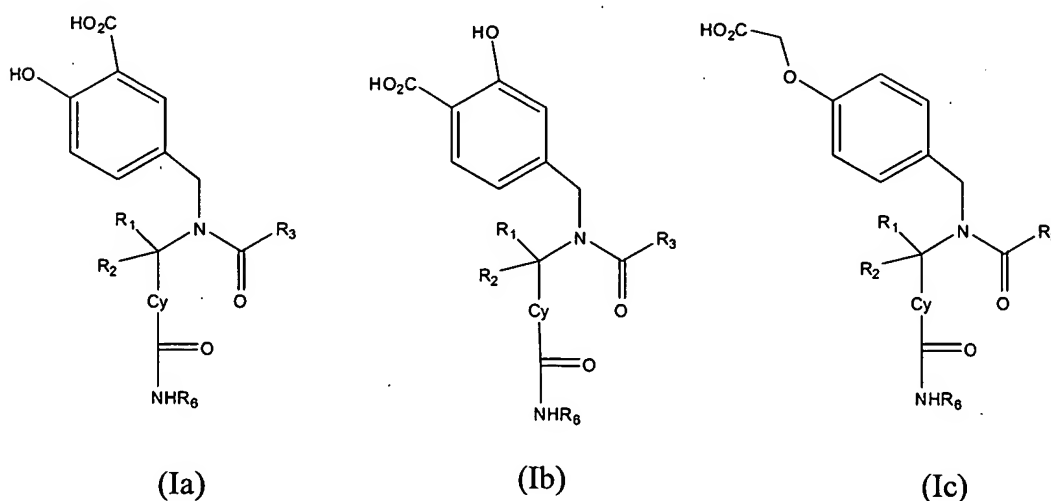
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(Guidelines for Examination of Patent Applications Under 35 USC 112, ¶1, "Written Description" Requirement, pg. 1105 column 3). For a claimed genus, the requirement may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to structural or chemical formulas, or disclosure of functional characteristics coupled with known/disclosed correlation between function and structure (Guidelines for Examination of Patent Applications Under 35 USC 112, ¶1, "Written Description" Requirement, pg. 1106 column 3).

5. Claims 10-14, 16, 17, 19-21 are rejected under 35 USC 112 1st paragraph as failing to comply with the written description requirement.

I. Scope of Claims

Scheme 1



Variables defined in claim 10 unless otherwise noted

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Claims 10 and 17

Compounds of Formula Ia, Ib, Ic and pharmaceutical compositions thereof

Claims 11 and 16

Compounds of Formula Ib, Ic and pharmaceutical compositions thereof

Claim 12Compounds of Formula Ia, Ib, Ic wherein $R_1=R_2=H$ Claim 13

Compounds of Formula Ia, Ib, Ic wherein Cy=phenyl, thiazolyl, phenyl-thiazolyl, and thiazolyl-phenyl

Claim 14Compounds of Formula Ia, Ib, Ic wherein: (i) Cy=phenyl, thiazolyl, phenyl-thiazolyl, and thiazolyl-phenyl and (ii) $R_6=C_{8-12}$ alkyl, C_1-C_4 alkyl phenyl optionally substituted by C_1-C_8 alkyl and phenoxyClaim 19Compounds of Formula Ib, Ic wherein $R_1=R_2=H$ Claim 20Compounds of Formula Ib, Ic wherein: (i) $R_1=R_2=H$; (ii) Cy=phenyl, thiazolyl, phenyl-thiazolyl, and thiazolyl-phenylClaim 21Compounds of Formula Ib, Ic wherein: (i) $R_1=R_2=H$; (ii) Cy=phenyl, thiazolyl, phenyl-thiazolyl, and thiazolyl-phenyl and (iii) $R_6=C_{8-12}$ alkyl, C_1-C_4 alkyl phenyl optionally substituted by C_1-C_8 alkyl and phenoxy*II. Scope of Disclosure*Reduction to Practice: a *limited* set of compounds *representing* following substituents:

- $R_1=$ H
- $R_2=$ H
- $R_3=$ (i) alkyl optionally substituted with amino
(ii) cyclopentyl/cyclohexyl/phenyl/pyridyl (attached directly or via alkylene/oxo), optionally substituted with cyano or fluoromethyl
- Cy= phenyl, thiazole-phenyl
- $R_6=$ phenyl (attached directly or via alkylene), phenyl-phenoxy, octyl

Reduction to Structural or Chemical Formulas:

It is noted that the disclosure lists possible substituents for all the variables in Markush style. However, this type of disclosure is not viewed in the art to be a representation of any of the species it entails. A “laundry list” disclosure of every possible moiety does not constitute a written description of every species in a genus because it would not “reasonably lead” those skilled in the art to any particular species. MPEP 2163.I.A. and *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1571, 39 USPQ2d 1895, 1905 (Fed. Cir. 1996).

Thus, there is no disclosure by reduction to structural/chemical formulas of species in addition to those reduced to practice.

Correlation between Structure and Function:

No correlation between structure and function is provided in the disclosure. Thus, it is not known what specific structural elements, shared by the genus of compounds claimed, are essential for the activity of these compounds as PTP1b inhibitors.

III. Analysis of Fulfillment of Written Description Requirement:

The predictability in the art is very low. In a structure/activity study of 3,4-Dephostatin derivatives, which are a class of inhibitors of PTP1B, Watanabe et al. found that the mere methylation of a hydroxyl substituent to the core structure lead to compounds with 100-200 fold increase in IC₅₀, dependent on the position of methylation (Watanabe et al., p. 744 Table 1). It was also found that the substitution of a

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nitrosamine moiety (N-N=O structure) by tetrazole (N-N=N structure) lead to complete loss of inhibiting power (Watanabe et al., p. 745, last paragraph).

Based on the disclosure by Watanabe et al., one of ordinary skill would not expect to obtain similar activity/property from the structurally diverse compounds instantly claimed that are not exemplified in the disclosure. For example, compounds containing the following substituents (non-exhaustively):

R₃= naphthyl, phenanthryl, furyl, triazyl, indolyl, piperidinyl, norbornyl
(optionally substituted)
Cy= norbornyl, piperidinyl, naphthyl-naphthyl, phenyl-indolyl
(optionally substituted)
R₆= spiro compounds, norbornyl
(optionally substituted)

In conclusion:

- (i) Substantial structural variation exists in the genus/subgenus embraced by claims 10-14, 16, 17, 19-21
- (ii) Disclosure of species supporting genus/subgenus is limited to compounds reduced to practice; disclosure not commensurate in scope with genus/subgenus claimed
- (iii) Common structural attributes of the claimed genus, combined with a correlation between structure and function, is neither disclosed in the instant application nor commonly known in the art.

Based on (i)-(iii), one of ordinary skill would reasonably derive that the inventor was, on the filing date, not in possession of the invention commensurate in scope with the claims.

(Enablement)

6. Claims 10-16, 17, 19-21 are rejected under 35 USC 112 1st paragraph as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916) which postured the question: is the experimentation needed to practice the invention undue or unreasonable? That standard is still the one to be applied. *In re Wands*, 858 F.2d 731, 737, 8USPQ2s 1400, 1404 (Fed. Cir. 1988). MPEP 2164.01(a) states "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue". The factors are applied below to the instant claims.

The breadth of the claims

The claims are drawn to products of Formula I with the scope as defined in section 5I, supra.

The nature of the invention

The genus of compounds are claimed to possess PTP1B inhibiting activity.

The state of the prior art/level of ordinary skill/level of predictability

The level of ordinary skill is high, but the level of predictability in the art is low, supra. There is no art known correlation between structure/function for this class of compounds. Absent guidance, one of ordinary skill would not know whether the compounds embraced by the claimed genus would possess PTP1B inhibiting activity.

The amount of direction provided by the inventor/existence of working examples

Example 1: tested and shown to possess PTP1B inhibiting activity

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Examples 2-53: it is unclear from the disclosure whether these compounds were tested for PTP1B inhibiting activity. Applicant is invited to submit an affidavit clarifying whether these compounds were tested and whether they possess PTP1B inhibiting activity.

The quantity of experimentation needed to make or use the invention

It is not known what compounds of the broad genus claimed, other than compound of Example 1, possess activity as inhibitors of PTP1B. The skilled artisan would be subject to undue experimentation to test the compounds for this activity before being able to practice the invention commensurate in scope with the breadth of the claims.

Allowable Subject Matter

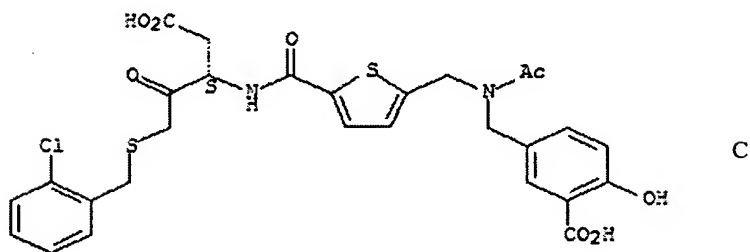
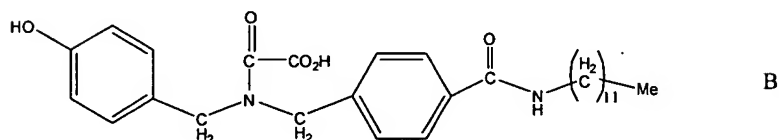
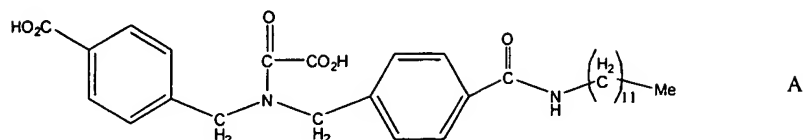
7. Claim 15 is allowable over the prior art for the following reasons. The closest prior art are the compounds shown in Scheme 2. Compounds (A) and (B) are taught by Swinnen et al. to be PTP1B inhibitors. The instant claims are structurally distinct from compounds A and B, respectively, due to the presence of an extra hydroxyl or carboxyl moiety to the phenyl ring. In view of the unpredictability in the art between structure and function, these modifications would not be obvious to one of ordinary skill.

Compound C is taught by Choong et al. to be a caspase-3 inhibitor. This compound fails to meet the structural limitation for compounds of formula Ia because of the presence of an ethyl moiety for variable R⁶ (C₆-C₁₅ alkyl claimed instantly for R⁶).

Claim 15 would be allowable if the rejection(s) under 35 U.S.C. 112 1st paragraph is overcome.

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Scheme 2



Conclusions

8. No claims are allowed.


9. Any inquiry concerning this communication should be directed to Sun Jae Y. Loewe whose telephone number is 571-272-9074. The examiner can normally be reached on Monday through Friday from 7:30 am to 5:00 pm.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Cecilia Tsang (571) 272-0562, can be reached. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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PRIMARY EXAMINER